Fusion of Three-Dimensional Echocardiographic Regional Myocardial Strain with Cardiac Computed Tomography for Noninvasive Evaluation of the Hemodynamic Impact of Coronary Stenosis in Patients with Chest Pain

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Background: Combined evaluation of coronary stenosis and the extent of ischemia is essential in patients with chest pain. Intermediate-grade stenosis on computed tomographic coronary angiography (CTCA) frequently triggers downstream nuclear stress testing. Alternative approaches without stress and/or radiation may have important implications. Myocardial strain measured from echocardiographic images can be used to detect subclinical dysfunction. The authors recently tested the feasibility of fusion of three-dimensional (3D) echocardiography–derived regional resting longitudinal strain with coronary arteries from CTCA to determine the hemodynamic significance of stenosis. The aim of the present study was to validate this approach against accepted reference techniques.

Methods: Seventy-eight patients with chest pain referred for CTCA who also underwent 3D echocardiography and regadenoson stress computed tomography were prospectively studied. Left ventricular longitudinal strain data (TomTec) were used to generate fused 3D displays and detect resting strain abnormalities (RSAs) in each coronary territory. Computed tomographic coronary angiographic images were interpreted for the presence and severity of stenosis. Fused 3D displays of subendocardial x-ray attenuation were created to detect stress perfusion defects (SPDs). In patients with stenosis >25% in at least one artery, fractional flow reserve was quantified (HeartFlow). RSA as a marker of significant stenosis was validated against two different combined references: stenosis >50% on CTCA and SPDs seen in the same territory (reference standard A) and fractional flow reserve < 0.80 and SPDs in the same territory (reference standard B).

Results: Of the 99 arteries with no stenosis >50% and no SPDs, considered as normal, 19 (19%) had RSAs. Conversely, with stenosis >50% and SPDs, RSAs were considerably more frequent (17 of 24 [71%]). The sensitivity, specificity, and accuracy of RSA were 0.71, 0.81, and 0.79, respectively, against reference standard A and 0.83, 0.81, and 0.82 against reference standard B.

Conclusions: Fusion of CTCA and 3D echocardiography–derived resting myocardial strain provides combined displays, which may be useful in determination of the hemodynamic or functional impact of coronary abnormalities, without additional ionizing radiation or stress testing. (J Am Soc Echocardiogr 2018;■:■-■.)

Keywords: Fusion imaging, Cardiovascular CT, 3D echocardiography, Vasodilator stress, Myocardium perfusion, Myocardial strain

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Abbreviations

3D = Three-dimensional

3DE = Three-dimensional echocardiography

CT = Computed tomographic

CTCA = Computed tomographic coronary angiography

CT-FFR = Fractional flow reserve from resting cardiac computed tomographic images

FFR = Fractional flow reserve

LAD = Left anterior descending coronary artery

LV = Left ventricular

SPD = Stress perfusion defect

In patients with chest pain, combined evaluation of coronary anatomy (i.e., presence and severity of stenosis) and its hemodynamic significance, namely, the presence and extent of ischemia, is essential. This is frequently addressed using downstream radionuclide myocardial perfusion stress testing in patients with abnormal findings on computed tomographic coronary angiography (CTCA), especially those with intermediate-grade stenosis.[1-5] This is because CTCA is known to overestimate the degree of stenosis and because the presence and extent of myocardial ischemia is more important than the severity of stenosis for identifying patients who would benefit from coronary revascularization.[6,7] Alternative approaches that do not involve stress and/or radiation may have important implications for greater patient safety and significant cost savings.

Another limitation of this diagnostic paradigm is that it is difficult to guarantee that hemodynamic or functional abnormalities are accurately attributed to stenosis in a specific coronary artery, because this requires one to mentally coregister these findings within the complex three-dimensional (3D) anatomy of the heart, given the wide interindividual differences in coronary anatomy. This is particularly problematic in the setting of multivessel disease, when it is unclear which artery is responsible for the symptoms. Fusion imaging may be helpful in this regard, because it provides a unique opportunity to simultaneously view different types of clinically relevant information in a shared space.[8-17] Specifically, in the context of significance of coronary stenosis, fusion imaging may allow the visualization of each coronary artery and any hemodynamic or functional parameter of interest mapped onto the underlying area of the myocardium, thus lending itself to direct identification of the culprit artery when an abnormality is present.

Several studies have shown that left ventricular (LV) strain derived from echocardiographic images can be used to detect dysfunction secondary to myocardial ischemia in the presence of normal ejection fraction and seemingly normal wall motion.[18-21] However, the vast majority of published studies that reported the use of myocardial strain to detect subclinical dysfunction were based on global strain measurements, while the usefulness of regional strain is considerably less well established and has been predominantly tested using two-dimensional strain analysis. In fact, the current guidelines state that there is insufficient evidence to support clinical use of regional strain.[22] In this study, we hypothesized that fusion of resting 3D echocardiography (3DE)–derived regional LV longitudinal strain with coronary arteries from CTCA might allow determination of the hemodynamic significance of coronary stenosis in patients with chest pain, without the need for additional radiation or stress testing. We recently tested the feasibility of this approach in a small study involving patients referred for computed tomographic (CT) coronary angiographic evaluation of coronary artery disease and found that resting strain abnormalities were more common when stenosis resulted in perfusion abnormalities under stress.[23] These findings suggested that resting regional LV strain abnormalities might be useful for identifying functionally significant coronary stenosis. The aim of the present study was to determine the accuracy of this approach in a larger group of patients with chest pain against a robust reference for hemodynamically significant stenosis.

METHODS

This was a prospective study in which we enrolled patients with chest pain referred for CTCA who agreed to undergo vasodilator stress computed tomography and transthoracic 3DE within 1 hour of CTCA. Figure 1 shows a diagram of the study design. Resting CT images were used for conventional detection of coronary stenosis as well as to extract the coronary tree for fusion. Vasodilator stress CT images were used to obtain perfusion data. Three-dimensional echocardiographic images were used to obtain the 3D endocardial surface and also analyzed to obtain strain data, which were mapped onto the 3D surface and fused with the coronary tree. In addition, stress CT perfusion data were also mapped onto the 3D endocardial surface and separately fused with the coronary tree. These fused displays were used to detect abnormalities in resting strain and stress perfusion defects (SPDs).

Because the choice of a robust reference technique that credibly reflects myocardial ischemia is not trivial, we evaluated several possibilities. One potential reference would be a combination of stenosis on CTCA and a SPD in the territory of the same artery, as a confirmation of its hemodynamic impact.[24-30] Another possibility is the recently developed and validated fluid dynamics based calculation of fractional flow reserve (FFR) from resting cardiac CT images (CT-FFR),[31-40] which is rapidly expanding into clinical practice.[41,42] Accordingly, this study was designed to validate resting strain abnormalities as a marker of hemodynamically significant stenosis against two reference standards: a combination of stenosis >50% on CTCA concomitant with an SPD, reflecting together the anatomic severity and the hemodynamic impact of stenosis (reference standard A),[43] and a combination of abnormal CT-FFR with an SPD in the same coronary territory, reflecting the hemodynamic impact in a more robust way than either one of its two components alone (reference standard B).

Population

We prospectively studied 78 patients (mean age, 55 ± 10 years; 46 men; 32 with hypertension; nine with diabetes mellitus; 37 with dyslipidemia; 24 with histories of tobacco use) with chest pain. Patients with relative contraindications to CTCA, including known allergies to iodine, renal dysfunction (creatinine > 1.6 mg/dL), inability to perform a 10-sec breath-hold, and contraindications to β-blockers or vasodilators, such as chronic obstructive pulmonary disease, advanced heart block, or systolic blood pressure < 90 mm Hg, were excluded. This group included the 27 patients reported in our previously published pilot study.[23] The study was approved by the institutional review board, and each patient provided informed consent before participation.

Three-Dimensional Echocardiographic Imaging and Analysis

Transthoracic 3D echocardiographic data sets were acquired at rest in the harmonic mode from a modified apical four-chamber view using the iE33 ultrasound imaging system (Philips Medical Imaging, Andover, MA) equipped with a matrix-array transducer